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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,894	12/15/1999	MARC PIECHACZYK	19141-007	5731

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/341,894	PIECHACZYK ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 national stage filing of PCT/FR98/00081, filed January 16, 1998 which claims benefit to foreign application FR 97/00540, filed January 20, 1997 in France.

Applicants' amendment filed April 21, 2003 has been received and entered. Claims 1-43 have been canceled. Claims 44-59 have been added. Claims 44-59 are pending and currently under examination.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, the embodiment of "the genetically modified cell does not cause disease in the subject following transplantation" is considered new matter. Applicants' support for the amendment set forth in the traversal of the 102 rejections is noted. Examiner acknowledges that the general objective of expressing an antibody in a subject is for the treatment and/or prevention

of cancer and viral infections, however this does not provide adequate support for the newly added claims. Review of the specification teaches that any cell type can be used, including several transformed cell lines (see for example page 14, lines 17-21). Further, of the cells specifically taught in the specification, it is noted that the C2C12 cell line is specifically claimed (see claims 46 and 54). However, a review of the relative art indicates that this cell line can result in tumor formation of myoblst origin even when the cells were encapsulated (see summary in abstract and second column on page 210, Hortelano *et al.* Haemophilia, 2001). Thus the specific cells taught as examples in the specification are capable of causing cancer in a subject. A review of the specification indicates that there is no guidance in choosing a cell that do not cause a disease or even a discussion to what would be considered the scope of disease. For example, the claims specifically encompass delivering an antibody to a human with C2C12 cells, however delivering these mouse cells to a human or any other species would result in a hyper acute rejection of the implanted foreign cells. It is noted that the specification teaches that several cell types have been successfully transfected with other transgenes and transferred into a subject and are set forth as preferred embodiments, however the only limitation to cell type contemplated as part of the invention is that it did not previously produce an antibody itself. The methods of monitoring pointed to by Applicants are also noted. Examiner acknowledges that certain guidelines in handling animals are generally required however these guidelines were not detailed in the specification. Moreover, they do not preclude the implantation of cells that cause disease which is often the subject of research. As noted by Applicants, [the guidelines could be construed to require monitoring for the comfort of the animal and euthanasia of animals developing tumors, however to this end, the guidelines would support that the types of cells

implanted could cause tumors or discomfort to the animal, and not the administration of cells that do not cause any disease. With respect to the specific methods of monitoring detailed in the specification, these are not methods of monitoring for disease, rather they monitor antibody production in the subject. The methods of monitoring set forth in the specification are to determine whether the subject produces the recombinant antibody or antibodies to the foreign antibody being produced by the recombinant cell, not a monitor of disease in the animal. Moreover, they are specifically set forth as a method for monitoring anti-idiotype response (Applicants' amendment page 14 and specification paragraph 97) which is not a indication of disease in general. Further, the methodology requires you to know the antigen, in this case the recombinant antibody that was expressed and does not teach an immunological survey of possible cancer antigens or disease state antigens. Examiner acknowledges Applicants' comments that gene therapy protocols may involve various types of monitoring, however no such protocols are taught in the instant specification. Additionally, the particulars of any monitoring protocol would be subject to the type of gene therapy one were performing. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966: "Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention."

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 44-59 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 44 and 52 are indefinite in the recitation of "suitable for the introduction into a subject" because what is considered suitable is not clearly set forth in the specification nor the claims. The suitability of a cell would be dependent on what was expected and where it was used. The suitability is relative to how the cell is used therefore subject to change. For example, a mouse cell may be suitable for implantation into a syngenic mouse but would not be suitable for implantation into a human.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Cirone *et al.* (Human Gene Therapy 14:1065-1077, July 2003) provides post-filing evidnece that C2C12 cells were used to express other types of transgenes and could be successfully implanted into animal models. However, unlike the instant specification where the recombinant cells are directly implanted into the subject, Cirone *et al.* teach the use of microencapsulation of recombinant cells.

Conclusion

No claim is allowed. Newly added claims are free of the art of record because while the art of record teaches cells and methods of making non-plasmocyte cells that produce antibodies and/or antibody fragments, each of the specific cells taught would most likely form a tumor when transplanted into any subject.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
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